**FMINUTES OF THE 66TH MEETING OF DRUGS TECHNICAL ADVISORY BOARD HELD ON 16TH JANUARY, 2014 IN THE CHAMBER OF DGHS, NIRMAN BHAWAN, NEW DELHI – 110002**

**PRESENT**

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| 1. Dr. Jagdish Prasad,<br>Director General of Health Services,<br>Nirman Bhawan, New Delhi. | Chairman |
| 2. Shri C. Hariharan<br>Director in-charge,<br>Central Drugs Laboratory,<br>Kolkata-700016 | Member |
| 3. Dr. S. D. Seth,<br>Advisor CTRI,<br>National Institute of Medical Statistics,<br>ICMR, Ansaari Nagar,<br>New Delhi-110002 | Member |
| 4. Dr. B. Suresh,<br>President, Pharmacy Council of India<br>New Delhi | Member |
| 5. Shri Satish Gupta,<br>Controller Drugs and Food,<br>J&K, Jammu | Member |
| 6. Dr. Dharam Prakash,<br>252, Dharam Kunj,<br>Sector -9, Rohini,<br>Delhi-110085 | Member |
| 7. Dr. A. K. Tiwari<br>Indian Veterinary Research Institute<br>Izatnagar-243122 (U.P.) | Member |
| 8. Dr. G. N. Singh,<br>Drugs Controller General (India)<br>FDA Bhawan, New Delhi-110002 | Member Secretary |

**CDSCO REPRESENTATIVES**

1. Shri A.K. Pradhan
   Deputy Drugs Controller (India)
   CDSCO, New Delhi
2. Shri Lalit Kishore
   Consultant, DCG(I)
   CDSCO, New Delhi
3. Shri R. Chandrasekhar,
   Deputy Drugs Controller (India)
   CDSCO, New Delhi

Dr. Sunil Gupta, Director, CRI, Kasauli, Dr. T. K. Chakraborty, Director, CDRI, Lucknow, Secretary, Medical Council of India, New Delhi, Dr. K. Chinnaswamy, Coimbatore, Dr. B.P.S. Reddy, Hyderabad, Dr. J. A. S. Giri, Hyderabad and Dr. Dhrubajyoti Bora, Guwahati, could not attend the meeting because of their pre-occupation.

Dr. G. N. Singh, Drugs Controller General (India) and Member Secretary DTAB welcomed the Chairman and members of the Board and requested the Chairman to initiate the proceedings as the quorum was complete.

**AGENDA NO. 1**

**ACTION TAKEN REPORT ON THE MATTERS ARISING OUT OF THE 65$^{TH}$ MEETINGS OF DRUGS TECHNICAL ADVISORY BOARD HELD ON 25$^{TH}$ NOVEMBER, 2013 AT NEW DELHI.**

The Board approved the Action Taken Report on the minutes of the 65$^{th}$ meeting held on 25$^{th}$ November, 2013. In the case of agenda no. 11 relating to the action to be taken in respect of FDCs licensed by the State Licensing Authorities and whose safety and efficacy has not been approved, it was decided that Dr. B. Suresh, President, Pharmacy Council of India will form a subcommittee in consultation with the Chairman to prepare guidelines for examination of such fixed dose combinations and the action to be taken in these cases as more than five thousand applications have since been received by the office of DCG(I). These guidelines will then be followed uniformly by the Expert Committees constituted for the purpose of examination of these applications.

## AGENDA NO. 2

## CONSIDERATION OF THE PROPOSAL TO AMEND THE DRUGS AND COSMETICS RULES, 1945 TO MAKE A PROVISION UNDER SCHEDULE K FOR UNBANKED DIRECTED BLOOD TRANSFUSION IN RURAL AREAS FOR NEEDY PATIENTS IN EMERGENCY SITUATIONS

The Member Secretary, briefed the members that the Ministry of Health and Family Welfare had received a representation from the Association of Rural Surgeons of India, Maharashtra, for making a provision under the Drugs and Cosmetics Rules, 1945 for "Unbanked Directed Blood Transfusion" in rural areas. The scarcity of blood banks in rural areas and non-availability of safe stored blood in a reasonable time and at affordable price results in loss of life in these areas. Surgeons, obstetricians and other qualified clinicians, now available in rural villages, are handicapped in saving precious lives due to non-availability of blood. The Association has therefore requested that the Drugs and Cosmetics Rules should be amended to make a provision for exemption of blood bank licence for hospital in rural areas for blood transfusion to the needy patients in emergency situations where no licensed blood banks are available. There is already an exemption provided under Schedule K of the Drugs and Cosmetics Rules, 1945 for Armed forces medical services in border areas, small mid-zonal hospitals including peripheral hospitals from the provision of taking blood bank licence subject to certain conditions. Similar exemptions may be extended for Unbanked Directed Blood Transfusion in rural areas also in emergency situations.

The proposal was considered in the 46$^{th}$ Drugs Consultative Committee meeting held on 12$^{th}$ & 13$^{th}$ November, 2013. It was recommended that the exemption under Schedule K could be granted to such hospitals provided it is consistent with the National Blood Policy and the centres are properly equipped to ensure safe blood transfusion in emergency cases and have facilities for testing and cross matching of blood. The exemption provided should simultaneously take care that there is no scope of misuse and the blood is collected for transfusion only.

The Chairman stated that Ministry of Health and Family Welfare, Government of India had earlier considered a proposal of opening of state of art blood banks in each district of the country where all the requisite test are done on the blood stored there and this blood is then distributed to the sub-centres for use by the hospitals. It was also decided that as a pilot project the state of art central blood banks will be setup in Delhi having latest testing facilities including Nucleic Acid Test (NAT) testing. The NAT test shortens the window period for detecting the viral markers in the blood. Such centralised blood banks shall supply blood to all sub-centres / PHC / CHC and hospitals. Further, it should also be ensured that a minimum quantity of all groups of blood is available at all the above centres. The use of ambulances to transport blood in emergency situations should also be explored. He further opined that views of the NACO and Red Cross Society should also be considered in this regard.

Shri Satish Gupta, Drugs Controller, J&K was of the view that each licensed blood bank has 2 to 3 storage centres attached to it for supply of blood to the nearby hospitals. He stated that he has not experienced any difficulty in supply of blood in his State. The exemption as proposed in Schedule K may result in supply of untested or poorly tested blood to the patients.

Dr. B. Suresh stated that many States have developed a system of Centralised drug procurement for supply of drugs throughout the State. Such a system could be replicated in the case of supply of blood also.

The members were of the view that the testing of the safe blood required lot of infrastructure and trained manpower. Poorly tested blood may result in transmitting many diseases. It would also be difficult to monitor the functioning of such centres. Moreover, exemption granted to the Armed forces hospitals, which function under a framework and in difficult terrain areas to undertake emergencies in the Armed Forces, cannot be compared to the exemption to the small centres or hospitals in the rural areas for blood transfusion by testing the blood in the centre itself prior to transfusion.

In view of the above DTAB did not agree to the proposed exemption and recommended that instead of having large number of centres testing the blood for transfusion, it is better to establish a system of Central Blood Bank in each district of the country with well equipped storage centres having properly tested blood to meet the requirements of rural areas.

## AGENDA NO. 3

**CONSIDERATION OF THE PROPOSAL TO AMEND RULE 122 DAC MAKING COMPULSORY PARTICIPATION OF THE STATE DRUGS INSPECTORS IN CLINICAL TRIAL INSPECTION BY AMENDING THE WORD 'MAY' TO 'SHALL' IN CLAUSE (h) OF THE RULE**

The member Secretary briefed the members that the Drugs and Cosmetics Rules, 1945 were amended under G.S.R. 63(E) dated 1st February, 2013 introducing rule 122 DAC relating to permission to conduct clinical trials. Under this rule it was provided under clause (h) that investigator, sponsor including his representative shall be open to inspection by the officers authorized by CDSCO who may be accompanied by an officer of the concerned State Drug Control Authority. The clause (h) is reproduced as under:

> "(h) The Sponsor including their employees, subsidiaries and branches, their agents, contractors and subcontractors and clinical trial sites and the investigator shall allow officers authorized by the Central Drugs Standard Control Organization, who may be accompanied by an officer of the State Drug Control Authority concerned, to enter with or without prior notice, any premises of Sponsor including their employees, subsidiaries and branches, their agents, contractors and subcontractors and clinical trial sites to inspect, search and seize any records, data, document, books, investigational drugs, etc. related to clinical trials and provide adequate replies to any queries raised by the inspecting authority in relation to the conduct of clinical trial."

In a meeting of the Secretary, Ministry of Health and Family Welfare with the Chief Secretaries / Health Secretaries of the State Governments and the administrator of the Union Territories on 13.08.2013 under the directions of the Hon'ble Supreme Court of India, in the case of Swasthya Adhikar Manch, Indore Vs. Government of India (W.P. Civil No. 33/2012), the role of the State Licensing Authorities in inspections of clinical trials was discussed. During the meeting the issue of making compulsory participation of the State Drug Inspectors in clinical trial inspections by amending the word 'may' to 'shall' in the above said provision was raised.

The matter was also deliberated in the 46$^{th}$ DCC meeting held on 12$^{th}$ & 13$^{th}$ November, 2013 and the members were of the view that the present provision is adequate and the amendment of the word 'may' to 'shall' in the provision is not considered necessary in the present circumstances.

The DTAB after deliberations recommended that status quo may be maintained as there is an overall shortage of Drug Inspectors available in the different States / UTs for carrying out their statutory duties. The Mashelkar Committee had recommended as one inspector for 50 manufacturing units and one inspector for 200 sales units for complying with the statutory duties prescribed under the Drugs and Cosmetics Rules, 1945. The number of Drug Inspectors available in many of the States is far short of these criteria. Moreover, the State Inspectors are required to be trained in monitoring of different aspect of clinical trials, trial protocol, role of Ethics Committees and violations of trial protocols before making any changes in the present provision. It was further, recommended that the DCG(I) may issue directions to the zonal / sub-zonal offices asking them that as far as possible an officer of the State Drug Control Authority concerned should accompany the inspection team whenever clinical trial inspection is carried out.

## AGENDA NO. 4

## CONSIDERATION OF THE PROPOSAL FOR AMENDMENTS IN SCHEDULE Y TO THE DRUGS AND COSMETICS RULES IN RESPECT OF APPROVAL OF CLINICAL TRIAL BY ETHICS COMMITTEES

The member Secretary stated that the Schedule Y to the Drugs and Cosmetics Rules, 1945 under **Para 2. 'Clinical trials'** sub para (1) lays down the requirements of the approval of the trial by the Licensing Authority as well as the by the Ethics Committee as under.

> *"Clinical trial on a new drug shall be initiated only after the permission has been granted by the Licensing Authority under Rule 21(b), and the approval obtained from the respective Ethics Committee(s). The Licensing Authority as defined shall be informed of the approval of the respective institutional Ethics Committee(s) as prescribed in Appendix VIII, and the trial initiated at each respective site only after obtaining such an approval for that site. The trial site(s) may accept the approval granted to the protocol by the Ethics Committee of another trial site or the approval granted by an independent Ethics Committee (constituted as per Appendix VIII), provided that the approving Ethics Committee(s) is/are willing to accept their responsibilities for the study at such trial site(s) and the trial site(s) is /are willing to accept such an arrangement and that the protocol version is same at all trial sites."*

The proposal to amend the clause to ensure that the Ethics Committee of the institute where the trial is proposed to be conducted is not bypassed as well as rights, safety and well being of the trial subjects are protected was earlier considered in the 60$^{th}$ meeting held on 10$^{th}$ October, 2011 also. The proposal was again placed before DTAB for consideration especially in respect of Bioequivalence or bioavailability studies.

The DTAB after deliberations recommended that the clause may be amended as under:

> "The clinical trials of new drugs are required to be conducted at the trial sites, which have their own Ethics Committees. The trial shall be initiated only after the permission has been granted by the Licensing Authority under clause (b) of rule 21, and the approval granted by the Ethics Committee of the institute where trial is proposed to be conducted. The Bioequivalence or bioavailability studies of drugs approved elsewhere and required for new drug approval in the country and of drugs approved in the country for marketing may be conducted at bioequivalence or bioavailability centres not having their own Ethics Committee. In such a case Ethics Committee approval may be obtained from an Ethics Committee in the same area and registered with the said licensing authority. In the case of a multi-centric clinical trial, where protocol version is the same at all trial sites, the Ethics Committee(s) of respective sites should accord their approval and accept responsibility for the study at the trial site prior to the initiation of the trial. The Licensing Authority shall be duly informed of the approval of the respective Ethics Committee(s) as prescribed in Appendix VIII".

## AGENDA NO. 5

## CONSIDERATION OF THE PROPOSAL TO AMEND THE DRUGS AND COSMETICS RULES, 1945 FOR MAKING IT MANDATORY TO SUBMIT POST MARKETING SURVEILLANCE DATA BY THE APPLICANTS FOR A PERIOD OF SIX YEARS

The member Secretary stated that the Schedule Y of the Drugs and Cosmetics Rules, 1945 under the "Post Marketing Surveillance" provides that the applicant is required to furnish the Periodic Safety Update Report (PSUR) for a period of four years. The PSUR shall be submitted every six months for the first two years after approval of the drug is granted to the applicant. For subsequent two years the PSUR need to be submitted annually. This condition is also incorporated under Form 45 & Form 46 as a condition for grant of approval / permission to import / manufacture a new drug formulation.

The Committee of Experts constituted under the Chairmanship of Prof. Ranjit Roy Chaudhury to lay down policies, procedures and SOPs in respect of approval of new drugs and clinical trials and banning / withdrawal of drugs have recommended that PMS for four to six years should be mandatory for all drugs permitted to be marketed in India. The recommendation was accepted by the Ministry of Health and Family Welfare for further consideration and making necessary amendment in the Drugs and Cosmetics Rules, 1945 for the purpose.

DTAB after deliberations felt that the present four year period for submission PSUR reports is adequate and status quo may be maintained in this regard.

## AGENDA NO. 6

**CONSIDERATION OF THE PROPOSAL TO AMEND THE DRUGS AND COSMETICS RULES, 1945 FOR MAKING IT MANDATORY TO SUBMIT APPLICATION TO MARKET NEW CHEMICAL ENTITIES IN THE CASES WHERE INDIA PARTICIPATED IN GLOBAL CLINICAL TRIALS OF THESE NEW CHEMICAL ENTITIES**

The member Secretary briefed the members that the Committee of Experts constituted under the Chairmanship of Prof. Ranjit Roy Chaudhury to lay down policies, procedures and SOPs in respect of approval of new drugs and clinical trials and banning / withdrawal of drugs, considered the issue of Indian participation in global clinical trials and gave the following recommendation:

> "India should participate in global clinical trials of NCEs to be used for diseases that are prevalent in our population. BA studies including pharmacokinetic and pharmacodynamic studies should also be conducted on the Indian population. After approval for marketing in the innovator country or in well-regulated developed country markets, approval should be sought from the DCGI for marketing these NCEs in India. After approval by the DCGI, these NCEs should be marketed in India speedily, preferably by production within the country. Ethnic and tribal population trials should be conducted before prescribing the NCE for such population groups."

It was therefore felt that if India participates in global clinical trials of New Chemical Entities (NCEs) to be used for diseases that are prevalent in our population, and if the drug is approved for marketing in the innovator's country or in any well-regulated developed country, the applicant should make application for marketing the NCE in India. After approval from the DCG(I) office, the NCE should then be marketed in India also.

The DTAB therefore recommended that an appropriate provision may be incorporated under the Drugs and Cosmetics Rules, 1945, so that it becomes mandatory for the applicant of the global clinical trial to submit an undertaking from the sponsor that as and when the new chemical entity is approved in the country of the origin or in a well developed country, the sponsor shall file application to the licensing authority as defined under clause (b) of rule 21, for permission for marketing the drug in the country.

**AGENDA NO. 7**

**CONSIDERATION OF THE PROPOSAL TO MAKE IT MANDATORY TO SUBMIT INFORMATION BY THE CLINICAL TRIAL APPLICANT REGARDING THE FINANCIAL PAYMENT TO BE MADE TO THE INVESTIGATOR FOR THE CONDUCT OF THE CLINICAL TRIAL**

The member Secretary briefed the members that a meeting of the Secretary, Health and Family Welfare with the Chief / Health Secretaries of the States / UTs and other State representatives was held on 13th August, 2013 to discuss all facets and aspects concerning the legal framework for strengthening the regulations of clinical trials and other incidental matters in compliance to the directions of the Hon'ble Supreme Court of India in the case of Swasthya Adhikar Manch, Indore Vs. Government of India (W.P. Civil No. 33/2012). During the course of meeting, the Secretary, Health and Family Welfare desired that some kind of provisions may be made under the Drugs and Cosmetics Rules, 1945 so that the information relating to the amount of money paid by the companies to Investigators for conduct of clinical trials is in the knowledge of the regulatory authorities.

The DTAB after deliberations agreed that a clause may be inserted in Schedule Y of the Drugs and Cosmetics Rules, 1945, under Para 1 relating to Application for Permission, that the information regarding the financial payment to be made to the investigator for the conduct of the clinical trial shall be furnished along with the application to the licensing authority as defined under clause (b) of rule 21.

Meeting ended with the vote of thanks to the Chair.

**(Extracts of the 66th DTAB minutes held on 16th January, 2014)**

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